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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,135	09/24/2003	Hong-Ji Xu	AND541/4-007US/58011	8671
21586	7590	09/08/2004	EXAMINER	
VINSON & ELKINS, L.L.P. 1001 FANNIN STREET 2300 FIRST CITY TOWER HOUSTON, TX 77002-6760			MOORE, WILLIAM W	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/670,135

**Applicant(s)**

XU ET AL.

**Examiner**

William W. Moore

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-75 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-75 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

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## DETAILED ACTION

### *Election/Restrictions*

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

1. Claims 1-10, drawn to a polynucleotide encoding the granzyme B amino acid sequence set forth in SEQ ID NO:3 - including SEQ IDs NOs:1 and 2 - to vectors comprising the polynucleotide, and to a first method of use thereof in making the polypeptide in a host cell transformed or transfected with the polynucleotide, classified, *inter alia*, in class 435, subclass 69.1.
2. Claims 13, 14, and 42, drawn to an isolated granzyme B having the amino acid sequence set forth in SEQ ID NO:3, and to a first of use of the protease in an assay method for identifying modulators of its activity, classified in class 435, subclass 226.
3. Claims 15-17, drawn to a method of use of an antisense compound to inhibit expression of a granzyme B in tissues or cells comprising contacting the tissues or cells with the compound, classified in class 536, subclass 24.5.
4. Claims 18, 19, and 22-24 draw in part to, and claim 20 drawn entirely to, a method of screening for neurological disorders by assessing the cellular expression of a granzyme B-encoding mRNA transcript, classified in class 435, subclass 6.
5. Claims 18, 19, and 22-24 draw in part to, and claim 21 drawn entirely to, a method of screening for neurological disorders by assessing the expression in cells of a granzyme B by detecting the protease, classified in class 435, subclass 7.4.
6. Claims 25 and 26, drawn to a method of screening for autoimmune diseases by assessing granzyme B expression with an unspecified agent, classified in class 435, subclass 4.
7. Claims 27-37, drawn to a second method of use of a polynucleotide encoding a granzyme B in inducing apoptosis in cells by introducing the polynucleotide into the cells, classified in class 514, subclass 44.
8. Claims 38 and 39 draw in part to, and claim 40 drawn entirely to, a method of detecting cells in an apoptotic or pre-apoptotic state by assessing cellular expression of a granzyme B-encoding mRNA transcript, classified in class 435, subclass 6.
9. Claims 38 and 39 draw in part to, and claim 41 drawn entirely to, a method of detecting cells in an apoptotic or pre-apoptotic state by assessing cellular expression a granzyme B by detecting its presence, classified in class 435, subclass 7.4.
10. Claims 43-45, drawn to a method of modulating endogenous granzyme B expression by regulating the expression of a tumor suppression gene which, absent any designation of an agent, is classified in class 514, subclass 1.
11. Claim 46, drawn to a method of modulating intracellular translocation of endogenous granzyme B by administering an adenovirus, classified in class 435, subclass 456.

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12. Claims 11, 12, and 47-50, drawn to a composition comprising, and to a gene therapy agent comprising, an expression construct and a nucleic acid sequence encoding the granzyme B amino acid sequence set forth in SEQ ID NO:3 - including SEQ IDs NOs:1 and 2 - and a method of treating a cancer by administering the expression construct to a patient, classified in class 435, subclass 320.1.

13. Claims 51-54 and 59, drawn to a method of inhibiting granzyme B by contacting tissues or cells with a composition comprising the inhibitor SPI-6, classified in class 514, subclass 2.

14. Claims 55-58 and 60, drawn to a method of inhibiting granzyme G by contacting tissues or cells with a composition comprising the inhibitor PI-9, classified in class 514, subclass 2.

15. Claims 61-66, drawn to a method of using a cell comprising a polynucleotide encoding the granzyme B amino acid sequence set forth in SEQ ID NO:3 - including SEQ IDs NOs:1 and 2 - to identify a modulator of granzyme B expression, classified in class 435, subclass 252.3.

16. Claims 67-70, a method of inhibiting a granzyme B with a modulator that inhibits expression of granzyme B which, absent any designation of a modulator, is classified in class 435, subclass 23.

17. Claims 71-73, a method of inhibiting apoptosis in a cultured stem cell by introducing a modulator capable of inhibiting granzyme B expression, classified in class 435, subclass 455.

18. Claims 74 and 75, drawn to progeny cells arising from less differentiated cells culture in the presence of a modulator capable of inhibiting granzyme B expression, classified in class 435, subclass 325.

The inventions are distinct, each from the other, because of the following reasons:

Inventions of Groups 1 and 2 are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product as claimed can be made by another and materially different process, such as solid-phase chemical synthesis.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 1 is unrelated to inventions of Groups 3-6 and 8-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, and different effects.

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Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Inventions of Groups 1 and 7 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP §806.05(h)). In the instant case the product as claimed can be used in a materially different process than the method of making a protease of Group 1, that of inducing cell death in Group 7.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 2 is unrelated to the inventions of Groups 3-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 3 is unrelated to the inventions of Groups 4-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 4 is unrelated to the inventions of Groups 5-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

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Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 5 is unrelated to the inventions of Groups 6-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 6 is unrelated to the inventions of Groups 7-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 7 is unrelated to the inventions of Groups 8-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 8 is unrelated to the inventions of Groups 9-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

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Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 9 is unrelated to the inventions of Groups 10-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 10 is unrelated to the inventions of Groups 11-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 11 is unrelated to the inventions of Groups 12-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 12 is unrelated to the inventions of Groups 13-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, or different effects.

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Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 13 is unrelated to the invention of Group 14. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions require the use of structurally distinct compounds are not disclosed as capable of use together and have different modes of operation.

Because these inventions are distinct for the reasons given above and the search required for Group 13 is not required for Group 14, restriction for examination purposes as indicated is proper.

The invention of Group 13 is unrelated to the inventions of Groups 15-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, and different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 14 is unrelated to the inventions of Groups 15-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, and different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

The invention of Group 15 is unrelated to the inventions of Groups 16-18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, and different effects.



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Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification restriction for examination purposes as indicated is proper.

The invention of Group 16 is unrelated to the inventions of Groups 17 and 18. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, and different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification restriction for examination purposes as indicated is proper.

The inventions of Groups 17 and 18 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP §806.04, MPEP §808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation, different functions, and different effects.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification restriction for examination purposes as indicated is proper.

A telephone call was made to Mr. Stephen M. Hash on August 26, 2004, to request an oral election to the above restriction requirement, but did not result in an election being made. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR §1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR §1.48(b) and by the fee required under 37 CFR §1.17(h).

#### *Notice of Requirements for Rejoinder*

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of**

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**right if the amendment is presented prior to final rejection or allowance, whichever is earlier.** Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. §§101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**


Further, note that the prohibition against double patenting rejections of 35 U.S.C. §121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

#### Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is now 571.272.0933. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can now be reached at 571.272.0928. The fax phone numbers for all communications for the organization where this application or proceeding is assigned remains 703.872.9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is now 571.272.1600.

William W. Moore  
August 27, 2004



PONNATHAPU ACHUTAMURTHY  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600